The most important chronic complications of type 2 diabetes are those affecting blood vessels and nerves.

The microvascular complications (retinopathy, nephropathy and neuropathy) are relatively specific to diabetes and the risk of these (particularly retinopathy) is used to help define the diagnostic criteria for diabetes. The risk of these complications is related to duration of diabetes as well as degree of hyperglycaemia. However, due to delayed diagnosis, these complications may already be present at diagnosis; and coexisting hypertension or dyslipidaemia may exacerbate their risk.

The macrovascular complications (coronary heart disease, cerebrovascular disease and peripheral vascular disease) are not specific to diabetes:

- Diabetes increases the risk of the development of macrovascular complications by 2–4 times. It also predisposes patients to more severe and generalised disease, and to onset of problems at a younger age.
- An increased risk of macrovascular disease is already apparent with degrees of hyperglycaemia below those reaching levels diagnostic of diabetes. For example, there is an approximate two-fold increase in risk of macrovascular disease in those individuals with IGT.
- Hyperglycaemia interacts with other risk factors, such as hypertension and dyslipidaemia, which also occur with increased frequency (30–50%).
- The coexistence of microvascular complications also exacerbates the severity of clinical manifestations. The very high relative risk of lower limb amputation in people with diabetes is an example of the effects of these interactions.

It is vitally important that hyperglycaemia, hypertension and dyslipidaemia are all controlled as effectively as possible to reduce the risk of development or progression of complications.

Once complications have become established, it is no longer sufficient just to treat hyperglycaemia and other risk factors, although this remains important. Additional measures such as laser photocoagulation, use of ACE inhibitors or angiotensin 2 receptor antagonists, foot care education, and treatment may all become necessary. Patients with macrovascular complications should also be considered for low-dose aspirin therapy if no contraindication is present.
Complications

Retinopathy

Type 2 diabetic patients can develop both proliferative and non-proliferative diabetic retinopathy, although it is the latter type complicated by macular oedema that is the leading cause of vision loss.

Every 1–2 years from diagnosis, patients should be checked for visual acuity by examining fundi through dilated pupils. In patients with established retinopathy or long duration of diabetes, examinations may need to be performed more regularly. When retinopathy is detected, fluorescein angiography may be required to assess the severity of retinopathy and the need for laser treatment. Adequate control of hyperglycaemia and hypertension is essential.

Nephropathy

Established diabetic nephropathy is best detected by the presence of 2+ proteinuria on dipstick urinalysis.

Proteinuria usually precedes the development of renal failure by several years as evidenced by rising serum creatinine concentrations. An increase in urinary albumin excretion rate, short of overt proteinuria, is known as ‘microalbuminuria’. This represents an early, subclinical phase of nephropathy and its presence indicates increased risk of progression to overt renal disease, as well as increased risk of macrovascular complications. Intervention at this point, with optimised glucose and blood pressure control, is particularly important to prevent or delay progression.

Although treatment of glucose and lipids remains important, the single most important aggravating factor in nephropathy is hypertension. Decline of renal function can be slowed by tight control of hypertension to levels below 140/80 mmHg (UKPDS data). A number of studies have also shown that either ACE inhibitors or angiotensin-2 receptor antagonists confer additional renoprotection over and above that obtained by blood pressure control alone. Thus, wherever possible one of these agents should be included in the antihypertensive regimen and their use as sole agents may also be considered in patients deemed to be normotensive.

Nephropathy is the single most critical determinant of overall prognosis, and this is particularly true in Asian and Pacific Island populations. In addition to renal failure, it is also associated with a greatly increased risk of macrovascular disease. However, with early and aggressive interventions as detailed previously, it should now be regarded as a potentially preventable complication.
Complications

Diabetic Foot Problems

Diabetic foot problems result from complex interactions between peripheral neuropathy (including autonomic dysfunction), microangiopathy and macrovascular disease, and poor foot hygiene. The relative contributions of each may vary from patient to patient and also may vary in different populations; for example, the contribution from peripheral vascular disease may be less in some Asian populations. As a result, lower limb amputation is one of the most feared complications of diabetes.

People with diabetes are, in general, 15–40 times more likely to require a lower limb amputation compared with the general population, and the comparative risk is even higher in elderly subjects. However, with aggressive management, a substantial proportion of amputations can be prevented.

Peripheral neuropathy with loss of pain sensation is the commonest cause of foot ulceration, closely followed by poor hygiene. This type of neuropathy and ulcer can be completely painless.

Peripheral vascular disease can also cause foot ulceration, which tends to be painful, and plays an important role in neuropathic ulceration by impairing healing. Neuropathic ulcers occur at sites of increased pressure, usually on the plantar surface of the foot. The most common reported site of neuropathic ulcers is the dorsum of the toes, and these are shoe induced. Callus develops as a result of the pressure (Figure 3).

For healing to occur, pressure needs to be reduced (e.g. by removal of callus, and wearing appropriate shoes or a pressure-relieving cast). Vascular ulcers tend to occur at the tips of the toes and on the heel (Figure 4).

For healing to occur, vascular supply may need to be improved. The infection must be treated aggressively, and antibiotic therapy is often required for many weeks or months. The important role of regular debridement of infected and necrotic tissue needs to be emphasised. Failure to heal an ulcer is the common underlying cause of subsequent amputation.
Complications

Routine checking of sensation and pedal pulses are the most important steps in identifying a foot that is at risk of ulceration. In the community, sensation is best tested with the 5.07/10 gm Semmes Weinstein Monofilament, which is a simple and inexpensive procedure. It is calibrated to buckle when a force of 10 gm is exerted (Figure 5).

If a patient cannot feel the pressure, the foot is considered to be insensate. Foot-care education for individuals identified at risk should be more detailed and practical than for other diabetic individuals with intact sensation and circulation.

Treatment of painful neuropathy is unsatisfactory. Useful measures include improving metabolic control and using simple analgesics, tricyclic antidepressants or anticonvulsants for pain relief. Reassuring the patient that pain is in fact not the underlying cause leading to amputation may be advisable.

If glycaemic control is very poor, foot infection and ulceration may occur as a result of poor hygiene, even in the absence of neuropathy or peripheral vascular disease. In this situation, apart from improving glycaemic control, it is important to advise patients to wear shoes to reduce the chance of trauma and, if they wear shoes, also to wear clean socks!

Practical aspects of assessing patients for complications.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
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<tbody>
<tr>
<td>Check visual acuity</td>
<td>Examine fundi through dilated pupils</td>
</tr>
<tr>
<td>Carry out urinalysis</td>
<td>Check for proteinuria. If present, serum creatinine should be determined. If proteinuria is not present, microalbuminuria should be determined</td>
</tr>
<tr>
<td>Record blood pressure</td>
<td>Palpate pulses of the feet. Use the Semmes Weinstein Monofilament to detect sensory loss. Examine the feet for cracks in the skin, fungal infection, condition of the nails, deformities and evidence of increased local pressure such as callus formation</td>
</tr>
<tr>
<td>Check sensation</td>
<td></td>
</tr>
</tbody>
</table>
Complications

Macrovascular Disease

In type 2 diabetes, 80% of all deaths are due to CVD. An increased risk of macrovascular disease is already present in individuals with IGT. Protection in pre-menopausal women is also lost when diabetes is present. In addition to the overall increased risk, people with diabetes develop more severe and generalised disease, which is associated with a worse prognosis and outcome. Coronary artery disease, cerebrovascular disease and peripheral vascular disease all occur more frequently as a result of diabetes, although ethnic differences may exist that determine which vascular territory is most prone to involvement.

It is important to be constantly on the alert for macrovascular disease. In addition, it should be remembered that, as a result of coexisting autonomic neuropathy, angina and myocardial infarction may be ‘silent’ due to the absence of pain. Unfortunately, also, ischaemic heart disease cannot easily be detected by physical examination.

Resting ECGs have limited value; thus, in patients thought to be particularly vulnerable (e.g. those with additional risk factors such as a strong family history, smoking, hypertension and dyslipidaemia), stress testing is necessary to evaluate cardiac disease.

Smoking greatly increases the risk of macrovascular disease. Control of hypertension and dyslipidaemia, and the use of low-dose aspirin are also effective strategies to reduce the risk of macrovascular events. Some studies, including the 4S study, have shown that the use of HMG-CoA reductase inhibitors to reduce cholesterol is effective in reducing macrovascular events and mortality in diabetic subjects, both with and without known ischaemic heart disease. The benefits appear to be even greater in diabetic subjects when compared with non-diabetic subjects. A common pattern of dyslipidaemia in people with diabetes is elevation of triglyceride with low HDL levels, but relatively unaffected total cholesterol. This pattern may be treated with fibrates, as demonstrated in the Diabetes Athero-Intervention Study (DAIS), although there are less data on the effectiveness of these drugs in reducing morbidity and mortality. Lifestyle measures should not be neglected.

In order to minimise the risk of macrovascular disease, it is essential to pay strict attention to all treatable risk factors. It is a mistake to focus on treating the hyperglycaemia alone.
Complications

The HOPE Study, amongst others, has also demonstrated the effectiveness of ACE inhibitors in the prevention of coronary events, and again the beneficial effect may be even more pronounced with diabetes.

Practical aspects of assessing and managing macrovascular disease:

- Always include evaluation of macrovascular disease and its risk factors in the assessment.
- Take a detailed history to determine the presence of angina, neurological symptoms, claudication and past episodes of vascular events. Listen for carotid bruit; palpate the pedal pulses; and measure blood pressure.
- Check urine for proteinuria and, in appropriate cases, microalbuminuria.
- Check cholesterol (LDL and HDL) and triglyceride levels.
- Help your patients to give up smoking.
- For secondary prevention, aggressively treat hypertension and dyslipidaemia.
- For primary prevention, aggressively treat hypertension and dyslipidaemia, especially in individuals who are considered to be at high risk of macrovascular events.

Diabetic subjects who suffer a myocardial infarction or stroke have a worse outcome than non-diabetic individuals, both during the acute phase and subsequently. In the context of myocardial infarction, the DIGAMI study has indicated improved short- and longer-term outcomes if intensive insulin therapy is used to establish good glycaemic control. Other preventative measures, such as the use of beta-blockers post-infarction, appear to be equally effective in people with diabetes when compared with the general population. Thrombolytic therapy in the acute phase appears safe in diabetes, even in the presence of retinopathy.